Pill Use Is Associated with Reductions in Overall Risk Of Cancer and in Risk of Main Gynecologic Cancers

Ever-use of the pill had no adverse effect on the overall risk of cancer in the large cohort of British women participating in the Royal College of General Practitioners' oral contraception study. Rather, analyses of data reflecting as much as 36 years of observation indicate that ever-users of oral contraceptives had a 12% reduction in the risk of developing any cancer and a 29% reduction in the risk of developing cervical, uterine or ovarian cancer. (Analyses of data from a subset of the cohort, however, revealed no association between ever-use and the risk of any cancer.) Long-term pill use was associated with elevated risks of some cancers and with reduced risks of others.[1] Analyses of data from the U.S. Nurses' Health Study, another long-term cohort study, confirm the inverse association between pill use and ovarian cancer risk; they also show that the risk of this disease is reduced among sterilized women and elevated among women who have used an IUD or are infertile.[2]

The British Study

The original British cohort comprised about 23,000 current pill users and a similar number of never-users recruited by general practitioners throughout the United Kingdom in 1968–1969. Participants were 29 years of age, on average, and were married or cohabiting at recruitment; most were white. They were followed up by their physicians, who collected information every six months about their pregnancies, illnesses, surgeries and use of hormonal contraceptives or hormone replacement therapy. One-quarter of women remained in the study until 1996. In addition, central registry data on cancer and mortality after the mid-1970s were available for three-quarters of the original cohort, regardless of whether the women were still being followed up by their physicians; these sources covered the period up to a woman's first cancer diagnosis or 2004, whichever came first.

Two data sets were used for the analysis of cancer risk. The main one was based on all women for whom central registry data were available and included about 744,000 woman-years of observation for ever-users of oral contraceptives and 339,000 woman-years of observation for never-users. The second one contained only information collected by general practitioners through 1996 and included about 224,000 and 331,000 woman-years of observation for ever- and never-users, respectively. Researchers calculated the rates of first diagnoses of a variety of cancers among ever- and never-users; rates were standardized for women's age and parity at diagnosis, and for cigarette smoking and social class (as defined by husband's occupation) at recruitment. Relative risks were calculated to compare rates by use status and selected characteristics of women.

Participants included in the main data set were predominantly younger than 40 when they entered the study (94% of ever-users and 90% of never-users); most had had at least one birth (83% and 80%, respectively) and had husbands who were employed in manual occupations (64% and 61%). Close to half of ever-users and four in 10 never-users in this data set smoked. Some 13% of ever-users and 10% of never-users in the general practitioner data set had used hormone therapy.

Compared with never-users of oral contraceptives, ever-users in the main data set had a 12% lower risk of developing any cancer during follow-up and a 29% lower risk of developing one of the main gynecologic cancers (cervical, uterine or ovarian cancer). They had significantly reduced risks of cancer of the large bowel or rectum (relative risk, 0.7), uterus (0.6) and ovaries (0.5), and of cancers for which the site was unknown (0.6) or that were classified as "other" (0.9). The reduction in overall risk translates into an estimated 45 cancers prevented per 100,000 woman-years. Relative risks calculated from the general practitioner data set were significant only for uterine and ovarian cancer (0.5 for each). In the main data set, the overall risk of cancer was significantly reduced for ever-users of the pill who were in their 30s or 50s, among both smokers and nonsmokers, among women of most parities and regardless of social class.

Data from the general practitioners' observations were used to explore the relationship between cancer risk and characteristics of women's oral contraceptive use. These analyses showed no relationship between pill use for less than four years and cancer risk (median duration of use was 44 months), and a modest decrease in overall risk associated with use for 4–8 years (relative risk, 0.9). However, use for more than eight years, which accounted for less than a quarter of use in the cohort, was associated with an elevated risk of any cancer (1.2) and of cancers of the cervix (2.7) and the central nervous system or pituitary (5.5). Furthermore, the trend toward increased risks of these specific cancers with increasing duration of use was statistically significant, as was a trend toward decreased risks of uterine and ovarian cancer.

Ovarian cancer risk was reduced for up to 15 years after women had last used the pill, and uterine cancer risk was reduced for up to five years since last use; for both of these cancers, the data suggest continued reductions in risk at longer durations since last use. Although trends for individual cancers were not statistically significant, ever-users' risk of developing any main gynecologic cancer declined as the elapsed time since last use of the pill increased.

The researchers comment that "many women, especially those who used the first generation of oral contraceptives many years ago, are likely to be reassured by [these] results." Nevertheless, they acknowledge that their findings may not reflect current pill users' experiences, given changes in preparations and in use protocols. Moreover, they emphasize that "the likely balance of cancer risks and benefits" may vary in different parts of the world, and that this is an important area for further study.

The U.S. Study

The initial cohort of the Nurses' Health Study consisted of almost 122,000 married, female registered nurses who were 30–55 years old at recruitment, in 1976. Baseline data, including information on oral contraceptive use and risk factors for cancer, were collected in a mailed questionnaire. In follow-up questionnaires sent to participants twice a year, women were asked about their cancer risk factors and newly diagnosed diseases; follow-up continued through May 2004. Until the mid-1980s, follow-up questionnaires assessed contraceptive use among premenopausal women; 1994 questionnaires asked again about sterilization. In 1980 and 1992, women were asked about infertility.

The 28 years of follow-up yielded information on 2.5 million woman-years of experience, including data on 612 women who developed ovarian cancer and for whom duration of pill use was known. Researchers examined ovarian cancer risk in relation to duration of pill use and time since last use in analyses controlling for age, body mass index, parity, age at menopause, duration of postmenopausal hormone use, and history of sterilization and smoking. They found that risk declined significantly with increasing duration of pill use; women who had taken oral contraceptives for more than 10 years were less likely than never-users to develop the disease (relative risk, 0.6). The relationship between risk and elapsed time since last use did not demonstrate a significant trend, but women who had last used the pill 5–10 years earlier had a reduced risk of ovarian cancer (0.5). Risk also was reduced for those who had used oral contraceptives for more than five years and had last taken the pill within the past 20 years (0.6); no protective effect was seen for women who had discontinued use longer ago. The researchers speculate that the "waning" of the protective effect could be problematic, since the incidence of ovarian cancer is highest after menopause.

Use of two other contraceptive methods also was associated with the risk of ovarian cancer. Women who had undergone tubal ligation had a reduced risk of this disease (relative risk, 0.7), and ever-users of an IUD had an elevated risk (1.8). Women reporting a history of infertility also had a somewhat elevated risk (1.4). The mechanisms underlying these associations are not well understood, as the researchers note, and require further investigation.—*D. Hollander*

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Methamphetamine Use Is Linked to Risky Behavior In Heterosexual Encounters

Methamphetamine use before or during a sexual encounter, which has a well-established association with risky behavior among men who have sex with men, may also be a predictor of risky behavior in heterosexual encounters. In a study conducted among injection-drug users in North Carolina, three of six risky behaviors examined were more likely to occur in heterosexual encounters involving use of the drug than in others; although use by one partner was not associated with elevated odds of any of these activities, use by both was associated with sharp increases in the likelihood of five of the six.[1]

The study was based on data collected between 2003 and 2006 from 703 men and women aged 18 and older who said that they had injected drugs in the previous 30 days and were not currently receiving treatment for substance abuse. With information participants provided about a total of 1,213 recent heterosexual encounters, the researchers used multivariate generalized estimating equations to assess relationships between methamphetamine use and six behaviors: unprotected vaginal intercourse, anal intercourse, unprotected anal intercourse, vaginal and anal intercourse during the same encounter, sex with a new partner and unprotected intercourse with a new partner. The analyses controlled for each partner's age, the male's race, cocaine use during the encounter and, for all behaviors except the two involving new partners, partner type (main or casual).

Participants were 41 years old, on average; the majority were male (73%), black (62%) and unemployed (71%). Half had graduated from high school, two in 10 were married or living with a partner, and one-third were homeless. Eleven percent said that they had used methamphetamine in the past 30 days, and 62–72% reported having used each of several other drugs (crack, alcohol, heroin, powder cocaine and marijuana). Some 27% had had multiple sex partners in the past 30 days, 39% had had unprotected vaginal intercourse and 9% had had anal sex.

At the bivariate level, recent methamphetamine users were more likely than nonusers to be white, homeless and unemployed, and were less likely to be high school graduates. During the past 30 days, they were more likely to have used other drugs, to have had more than one sexual partner or a partner who injected drugs, and to have engaged in anal intercourse.

Nearly all sexual encounters (89%) involved vaginal sex, and 9% involved anal intercourse; in slightly more than half of each of these types of encounter, the couple did not use condoms. Eighteen percent of encounters involved no substance use, 28% involved use by one partner and 54% use by both. Alcohol was the most commonly used substance (reported in 56% of sexual encounters), and methamphetamine the least (7%).

In the multivariate analysis, any methamphetamine use before or during a sexual encounter was associated with a roughly doubling of the odds of three risky behaviors: anal intercourse (odds ratio, 2.4), both vaginal and anal intercourse (2.4) and sex with a new partner (2.0). However, results were strikingly different in separate analyses examining encounters involving one partner's and both partners' use of methamphetamine. Use by only one partner was not associated with any of the risky behaviors studied, but use by both partners was associated with an increased likelihood of four of the six: anal intercourse (4.7), both vaginal and anal intercourse (3.7), sex with a new partner (5.0) and unprotected sex with a new partner (5.0).

The researchers note that event-level analyses of substance use and heterosexual activity have been rare, and that more such studies will be key to creating effective STD prevention interventions that "address the possibility of multiple and varied sex acts—thus, multiple and varied infection risks—during any single encounter." Meanwhile,

they conclude, health professionals who provide care to methamphetamine users should work toward "developing strategies and messages. . .for reducing risks associated with sex while using methamphetamine."—*D. Hollander*

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Provider Advice to Women May Vary by Women's Social Class and Ethnicity

Low-income black and Latina women surveyed in the Los Angeles area were more likely than middle-class whites to say that during a current or recent pregnancy, a health care professional had advised them to limit their childbearing.[1] In a multivariate analysis of the survey results, ethnicity and social class were the only characteristics associated with the odds that women had received this kind of advice. Low-income Latinas (along with women who had large families and unmarried women) also had elevated odds of saying that their doctor or someone else had discouraged them from having children.

The survey sample consisted of 193 low-income and 146 middle-class women who were pregnant or had given birth in the previous five years. Women were considered low-income if they were on welfare, had health coverage through Medi-Cal (California's Medicaid program) or were uninsured; low-income participants were recruited at offices of the Special Supplementary Food Program for Women, Infants and Children. Women were classified as middle-class if they had a college or graduate degree and had health insurance other than Medi-Cal; these women were recruited at a variety of locations in middle-class neighborhoods and through electronic mailing lists.

Survey questions covered women's demographic characteristics, their sources of reproductive health care and the topics they discussed with reproductive health care providers. Women's reproductive health care experiences during pregnancy were measured through two scales: a three-item scale assessing restrictive recommendations regarding childbearing; and a four-item scale assessing discouragement of motherhood. Scores above the median on the first were taken to mean that women felt that their doctor or another medical professional had advised them to limit their childbearing, and scores above the median on the second were interpreted as an indication that women felt that their doctor or someone else had discouraged them from having children. Researchers used logistic regression to identify characteristics associated with these outcomes.

The low-income participants were 26 years old, on average; 33% were Latina, 26% were black, 26% were white and the rest reported a variety of other racial and ethnic backgrounds. Most were unmarried (68%), had a high school education or less (58%), and had an annual household income of less than $20,000 (73%). By contrast, the middle-class respondents were, on average, 35 years of age; 50% of these women were white, 16% Latina, 12% black and the remainder of other racial or ethnic backgrounds. The great majority were married (86%) and reported an annual household income of more than $40,000 (95%); this group was about evenly divided between women who had only a college degree and those who had a higher degree. Most women in both social class groups had one or two children; low-income women were more likely than middle-class respondents to have three or more.

Individual experiences that made up the restrictive recommendations scale were not widely reported: Thirteen percent of women said that while they were pregnant, a doctor or other health care provider had often or very often discussed with them the importance of limiting family size; 7–8% reported that a provider had often or very often talked with them about their undergoing sterilization or their partner's having a vasectomy. Reports of experiences pointing to discouragement also were not common. Only 3% of participants said that they had often or very often felt that their doctor did not want them to have a child or that their doctor had tried to persuade them not to do so; 74% had generally considered their doctor supportive of their decision to have a baby, and 78% said that others were supportive of the pregnancy. The possible range of scores for each scale was 1–5, and the median score on each was 1.3, indicating relatively little experience with restrictive recommendations and discouragement.

The likelihood that a woman reported having received advice to limit her childbearing was significantly higher among low-income blacks and low-income Latinas than among middle-class whites (odds ratios from multivariate analysis, 3.2 and 3.4); no other characteristics included in the analysis (age, parity and marital status) were associated with having received such advice. Low-income Latinas also were more likely than middle-class whites to say they had been discouraged from having children (2.6). Parity and being unmarried were positively associated with women's odds of having felt discouraged by their doctors' and others' support during their pregnancy (1.3 and 2.4, respectively).

While acknowledging the shortcomings of the sample and other methodological limitations, the researchers conclude that their study "provides insight into how low-income women and women of color perceive the care they receive and the role of health care providers in unequal treatment in reproductive health care." They recommend several avenues for further study, including direct investigation of providers' attitudes toward low-income patients and "how negative health care experiences affect women's trust in the health care system and their providers, and how such issues affect willingness to seek care."—*D. Hollander*

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Breast-Feeding: Support Interventions Associated With Increased Practice

In a randomized controlled study conducted in Singapore, women who received prenatal education and those who received postnatal support were significantly more likely than those who received only routine obstetric care to be breast-feeding exclusively at six months (relative risks, 2.2 and 2.1, respectively).[1] Compared with those in the routine-care group, women in the prenatal intervention group were more likely to be exclusively breast-feeding at six weeks and

three months (1.7 and 1.9, respectively); similarly, women in the postnatal intervention group were more likely than those in the routine-care group to be breast-feeding exclusively at two weeks, six weeks and three months (1.8, 1.9 and 1.9, respectively). Of the two strategies, postnatal support had slightly stronger associations with rates of any breast-feeding.

The World Health Organization recommends exclusive breast-feeding—that is, breast milk only, without formula or water—for the first six months of an infant's life and partial breast-feeding for up to 24 months thereafter. However, relatively few women are able to establish and maintain the practice. To determine whether professional support could help women initiate and maintain breast-feeding, researchers recruited 450 healthy pregnant women attending prenatal clinics at a tertiary hospital in Singapore between February 2004 and May 2006. The women were eligible if they delivered at 34 weeks or later, intended to breast-feed and had no illness that would prevent them from doing so. The women were randomized into three groups: those who received routine obstetric care only; those who also received one prenatal breast-feeding education session that included the opportunity to speak to a lactation consultant; and those who also received two sessions of postnatal lactation support (one before discharge and the other at the first postnatal visit). At a baseline prenatal interview, the women were asked about their demographic characteristics and prior experiences with breast-feeding; they were also given a diary to track infant feeding for six months. The researchers examined the rates of exclusive, predominant, partial and no breast-feeding at two-week, six-week, three-month and six-month follow-up interviews; modified Cox regression analysis was used for pairwise comparisons of breast-feeding rates across study groups. Descriptive statistics were analyzed on an intention-to-treat basis.

The mean age of the women was 29.4 years, and 90% had household incomes of less than S$5,000 (US$3,294). Sixty-four percent of the women had a primary education or less, and 60% had had more than one child; 56% had breast-fed previously. Across the three study groups, the most common mode of delivery (76% vaginal births), mean gestational age (39.2 weeks) and mean birth weight (3,179 g) were also similar.

At six weeks, 17% of women receiving routine care only and 29% of those in the prenatal intervention group were breast-feeding exclusively. Those proportions were 13% and 24%, respectively, at three months, and 9% and 19% at six months. Those receiving the prenatal intervention were significantly more likely than those receiving only routine care to be practicing exclusive breast-feeding at six weeks, three months and six months, with relative risks of 1.7, 1.9 and 2.2, respectively.

Among women who received the postnatal intervention, 38% were breast-feeding exclusively at two weeks, 31% at six weeks, 24% at three months and 22% at six months. The proportion exclusively breast-feeding was significantly higher in the postnatal intervention group than in the routine-care group at all four points, with relative risks of 1.8, 1.9, 1.9 and 2.1, respectively.

Although there was no significant difference in the rate of exclusive breast-feeding at two weeks between women in the postnatal intervention group and women in the prenatal intervention group, women who had received the postnatal intervention were more likely than those who had received the prenatal intervention to be exclusively or predominantly breast-feeding (relative risk, 1.5). In addition, the proportion practicing any type of breast-feeding at six weeks was higher in the postnatal intervention group than in either of the other groups (1.2 each).

According to the authors, the "lack of breast feeding is significantly associated with higher use and cost of health care," and promotion of the practice leads to "improved short and long term health of breast fed children [and] improved wellbeing for mothers who have breast fed." They suggest that "future research. . .compare the specific cost effectiveness of. . .strategies for improvement of breast feeding practice."—*L. Melhado*

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Despite Differences in Legal Status, Abortion Occurs At Similar Rates in Developing and Developed Countries

An estimated 42 million abortions occurred throughout the world in 2003, and although the vast majority were in developing countries, where abortion laws generally are restrictive and unsafe procedures common, overall abortion rates were similar in developed and developing countries—26 and 29 per 1,000 women of reproductive age, respectively. Nearly half of abortions were unsafe procedures, which occurred at a rate of 16 for every 1,000 women aged 15–44 in developing countries and two per 1,000 women in developed countries. These findings are part of the picture painted by the first comprehensive assessment of abortion worldwide since 1995.[1]

The researchers gathered data on safe abortions—"those that meet legal requirements in countries in which abortion is legally permitted under a broad range of criteria"—from official national reporting systems, nationally representative surveys and published reports. They examined the quality of the data and corrected for underreporting of abortions when the data appeared to be incomplete. To estimate the incidence of unsafe abortions—procedures performed "by people lacking the necessary skills or in an environment that does not conform to minimum medical standards"—they relied mainly on data from hospital records, surveys and published studies. United Nations population and birth estimates were used for the calculations of abortion rates and ratios.

Worldwide, 42 million abortions took place in 2003—29 for every 1,000 women of reproductive age. Both the number and the rate represent declines from 1995, when an estimated 46 million abortions occurred, yielding a rate of 35 per 1,000 women; the rate declined more sharply in developed than in developing regions. The great majority of abortions in 2003 (35 million) were in developing countries, but the overall rate differed little between developed and developing countries (26 and 29 per 1,000, respectively). At the regional level, greater variation in rates was evident. Rates were 28–31 per 1,000 in Africa, Asia, Europe, and Latin America and the Caribbean, but only 17–21 per 1,000 in Northern America and Oceania. Moreover, differences within regions were often dramatic. Whereas Northern, Southern and Western Europe had overall abortion rates

of 12–18 per 1,000, Eastern Europe, which registered the greatest decline among developed areas, had a rate of 44 per 1,000 (the highest of any subregion). In Asia, rates ranged from 24 (in the western part of the region) to 39 (in the southeast).

Almost 20 million abortions in 2003 (nearly half of the worldwide total) were unsafe procedures, and 97% of these occurred in developing countries. Unsafe procedures made up more than half of all abortions in the developing world, but fewer than one in 10 in developed countries. Fourteen unsafe abortions occurred per 1,000 women worldwide—16 per 1,000 in developing countries and two per 1,000 in developed ones. In Africa and in Latin America and the Caribbean, where abortion laws are highly restrictive, 29 unsafe abortions occurred per 1,000 women; by contrast, rates were 11 per 1,000 in Asia and at most three per 1,000 in the remaining regions. Even within the regions with the highest overall levels of unsafe abortion, however, incidence varied. Rates ranged from 18 to 39 per 1,000 in Africa, from 16 to 33 in Latin America and the Caribbean, and from eight to 23 in Asia.

The 22 million safe abortions that occurred worldwide represented a rate of 15 per 1,000 women, or 24 and 13 per 1,000 in developed and developing countries, respectively. Rates of safe abortions per 1,000 women were 15 in Oceania, 18 in Asia, 21 in Northern America and 25 in Europe. In most of Europe, rates were below 20 per 1,000, but in the eastern part of the region, 39 safe abortions occurred per 1,000 women. Virtually no abortions in Africa or in Latin America are considered safe procedures.

For every 100 live births worldwide in 2003, an estimated 31 abortions occurred—16 safe and 15 unsafe procedures. This measure, the abortion ratio, varied widely among and within regions. It was as low as 17 in Africa (likely reflecting the region's high fertility levels), but was about twice that in Asia, in Latin America and the Caribbean, and in Northern America; it reached 59 in Europe. Abortion ratios ranged from 14 to 24 per 100 live births in Africa, from 22 to 51 in Asia, from 26 to 42 in Latin America and the Caribbean, and from 23 to 105 (signifying that abortions outnumbered live births) in Europe.

In all, 20% of pregnancies ended in abortion in 2003, including 28% of those in the developed world and 19% of those in developing countries. The proportion was lowest (12%) in Africa and highest (32%) in Europe. Similarly, at the subregional level, it ranged from one in 10, in Middle Africa, to nearly half, in Eastern Europe.

The researchers observe that the safety of abortion largely reflects its legal status, but "unrestrictive abortion laws do not predict a high incidence of abortion, and. . .highly restrictive abortion laws are not associated with low abortion incidence." Unsafe abortions may occur in countries with liberal laws, they suggest, because information or access to safe medical services is poor. And although some abortions in restrictive environments are performed safely, most are performed in settings that pose high risks to a woman's health and well-being. Noting that unintended pregnancy is the "root cause" of abortion, the researchers point out that continued assessments of unintended pregnancy, abortion and consequences of unsafe abortion will "help establish where service improvements are most needed."—*D. Hollander*

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The More Obese a Woman Is, the Greater Her Risk Of Having a Stillbirth

Obese women are more likely than their normal-weight counterparts to have a stillbirth, and the risk appears to rise with the degree of a woman's obesity.[1] Overall, Missouri women who gave birth between 1978 and 1997 were about 40% more likely to have a stillbirth if they were obese than if they were normal-weight; the risk of stillbirth was elevated by 30% for women at the low end of the obese range, but was nearly doubled for the extremely obese. The general pattern of increasing risk with more severe obesity held for both black and white women, but the differentials were greater for blacks in every category.

Given a "persistent surge" in extreme obesity among women, and well-established connections between obesity in general and poor birth outcomes, researchers set out to explore the relationships between stillbirth risk and degrees of obesity. They used linked data files from Missouri's vital statistics system to study maternal characteristics and birth outcomes associated with singleton pregnancies of 20–44 weeks' gestation. After calculating women's prepregnancy body mass index (or BMI, defined as weight in kilograms divided by the square of height in meters), they categorized women according to the following weight categories: normal (BMI, 18.5–24.9), class 1 obesity (30.0–34.9), class 2 obesity (35.0–39.9) and extreme obesity (40.0 or higher). (Women who were underweight or who were overweight but not obese were excluded.) Stillbirth was defined as in utero fetal death at 20 or more weeks' gestation; the researchers computed stillbirth rates, compared them across maternal characteristics by using chi-square tests and used Cox hazards regression to assess risk factors.

Approximately 1.4 million mother-fetus pairs were included in the analyses. Nearly 10% of women were obese: Six percent were at the low end of the obesity range, 2% were in the middle and 1% were at the high end. The proportion who were obese was higher among black women than among whites—13% vs. 9%. Obese women were more likely than those of normal weight to be at least 35 years old, multiparous and black; they had had more schooling than normal-weight women and were more likely to have received adequate prenatal care. Normal-weight women were more likely than their obese counterparts to be married and to smoke.

The frequency of common medical and obstetric complications differed between obese and normal-weight women. Diabetes, chronic hypertension, preeclampsia and eclampsia occurred more often among obese than among normal-weight women; anemia and placental disorders were more frequent among normal-weight women than among those who were obese.

In all, 8,240 stillbirths occurred during the study period, most of them (86%) to normal-weight women. The stillbirth rate was significantly higher among obese women than among those with a normal weight—8.5 vs. 5.5 per 1,000 live births plus stillbirths. Rates also varied by category of obesity, rising from 7.8 per 1,000 for women in the class 1 group to 8.7 per 1,000 for those in class 2 and 11.7 per 1,000 women who were extremely obese.

Obese women overall had a 40% greater risk than normal-weight women of having a stillbirth (hazard ratio, 1.4). Moreover, the differential climbed steadily and significantly with BMI: The increase in risk was

30% among women at the low end of the obese range, 40% among those in the middle and 90% among those at the high end.

Separate analyses by race revealed that the stillbirth rate was higher among black obese women than among white obese women (11.4 vs. 7.8 per 1,000 live births plus stillbirths). Stillbirth risk was directly associated with BMI in both groups, but the magnitude of risk was greater for blacks than for whites. Obese black women overall were almost twice as likely as their normal-weight counterparts to have a stillbirth (hazard ratio, 1.9); the increase was 60% among the least obese women, 90% among the moderately obese and 130% among the extremely obese. For whites, by contrast, the overall increase in risk for obese women was 40%, and the differential rose from 30% to 80% with increasing BMI. The investigators speculate that these differences reflect racial disparities in rates of "obesity-related morbidities."

According to the researchers, although their analyses may have been affected by the aggregation of different cohorts, controls that they included for year of birth should have largely eliminated the potential bias, and the study's use of population-based data makes the results "reasonably generalizable." They remark that their findings should be seen "as impetus for more refined studies that will potentially offer answers to many questions emanating from these preliminary results."—*D. Hollander*

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Circumstances of Women's First Birth May Be Linked to Their Health During Middle Age

Once women reach late middle age, their mortality and disease risks may be related to their early childbearing history, according to analyses of data from the Health and Retirement Study (HRS), which conducts periodic surveys to track participants' health, socioeconomic circumstances and family structure.[1] Among U.S. women who were born in 1931–1941 and lived until at least the early 1990s, those who had first given birth as teenagers had elevated odds of dying between 1994 and 2002; they also were more likely than others to have had heart disease, lung disease or cancer by 1994. Women who had had a nonmarital first birth appeared to be at risk of early mortality, but the association lost significance when midlife socioeconomic status was taken into account.

HRS participants were first interviewed in 1992, when they were 51–61 years of age, and are reinterviewed every two years. The data set includes information on women before they gave birth, at the time of their first birth and during midlife. To assess the relationship between childbearing history and mortality in late middle age, the analyst examined data for 1994–2002, which were linked to national mortality statistics. Assessment of a variety of diseases was based on data from the 1994 survey.

In all, 4,335 women were included in the analyses. Most were U.S.-born and white; their average age was 56 at the time of the first survey, and they had had a mean of 12 years of schooling. In 1994, 69% of women were married, and most of the rest were divorced (13%) or widowed (12%). Also at that time, 41% of participants said that they had been told that they had high blood pressure, 10–13% had ever received a diagnosis of diabetes or heart or lung disease, 9% had had cancer and 3% had suffered a stroke. During the years for which mortality data were examined, 3% of women married, 9% became widows and 2% divorced.

Ninety-two percent of cohort members had had children; 83% had had more than one. One-quarter of parous women had first given birth as teenagers, and one in 10 had been unmarried at the time of their first birth. Four percent had given birth after age 39, and 36% had had a birth interval of less than two years. Parous women were generally similar to the overall cohort in terms of measures used in the analyses.

According to results of Cox regression analyses, women's risk of dying between 1994 and 2002 rose significantly with increasing age and declined with increasing education, net worth and income; it was lower among women who were never-married in 1994 than among those who were married at the time. Results were essentially the same for parous women as for the cohort in general. In addition, parous women had an elevated mortality risk if they had given birth before their 20th birthday (hazard ratio, 1.6), and this relationship remained significant even after midlife socioeconomic circumstances were controlled for (1.4). In an initial regression, the risk of dying was elevated among women who had been unmarried at first birth (1.6); this association remained in analyses that adjusted for background characteristics that preceded first birth, but it lost significance in the final model, which added controls for midlife socioeconomic characteristics.

A series of logistic regression models controlling for background and midlife characteristics indicated that women who had given birth before age 20 were at increased risk of having had heart disease, lung disease or cancer by 1994 (coefficients, 0.3–0.4). Those who had had a nonmarital first birth were at increased risk for heart disease and stroke (0.4 and 0.6, respectively). Two reproductive history characteristics that were not significant predictors of mortality were associated with midlife health: The risk of heart disease was reduced among women who had given birth after age 39 (−0.6) and among those who had had a birth interval of less than two years (−0.3).

The analyst notes that the wide range of measures available from the HRS allows the most comprehensive examination ever of the relationships between childbearing history and later health and mortality. Nevertheless, he observes that three central questions remain: whether the association between early childbearing and mortality would be affected by the inclusion of additional background measures; whether the findings related to childbearing outside marriage would be the same for later cohorts, among whom nonmarital childbearing has been more common than it was for the HRS cohort; and how childbearing history is related to mortality throughout the life course. Studies on these issues, he concludes, would bring a greater understanding of the relationship between childbearing history and women's later health. *—D. Hollander*

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Participants in HIV Vaccine Trials May Experience Negative Social Effects

One in five volunteers in a multicenter HIV vaccine efficacy trial reported that their participation had at least one negative social impact in a three-year period.[1] The overwhelming majority of negative experiences involved difficulties in interpersonal relationships; reports of problems with insurance or employment were rare. More than nine in 10 of the volunteers were men; for them, reports of negative events were associated with being 35 or younger, having more than one partner, participating at a study site that enrolled no more than 50 volunteers and participating at a site located in a city with a high AIDS prevalence.

The study, known as Vax004, was a randomized, placebo-controlled trial conducted at 57 sites in the United States, three in Canada and one in the Netherlands. Over a 17-month period beginning in 1998, a total of 5,417 individuals at risk of HIV infection—5,108 HIV-negative men who have sex with men and 309 women—enrolled. Participants were followed up for 36 months; every six months, they completed interviews that assessed the social impact of taking part in the trial. Interviewers asked about potential negative impacts involving personal relationships, unintentional disclosure of participation in the trial, employment, life and disability insurance, health insurance, housing, medical care, government agencies, travel and immigration, and unspecified other issues. Participants who acquired HIV infection during the trial had medical visits every four months for two years and were asked about social impacts at these visits as well.

Male participants were predominantly white (86%) and had at least a college education (64%); their average age was 36. Forty-four percent had had an HIV-infected partner in the six months before their baseline interview; the median number of partners in that interval was five. About half of male volunteers were enrolled at sites in cities with a medium-size population (more than 150,000 and less than 750,000), and about half were at sites located in cities with a medium prevalence of AIDS (more than 3,230 and fewer than 21,658 cumulative cases); six in 10 were enrolled at sites that had more than 100 trial participants.

Female volunteers were 37 years old, on average; most were black or Latino (69%) and had no more than a high school education (83%). Women's median number of partners in the six months before enrollment was two; 42% had had an HIV-positive partner during that time. Close to six in 10 women were enrolled in sites in large cities, and a similar proportion were in cities where the cumulative number of AIDS cases was high (21,658 or more). Sixty-two percent were enrolled at sites with more than 100 volunteers.

Overall, 18% of volunteers experienced at least one negative social impact of trial participation; 3% experienced two or more. The most common problem was negative reaction from friends, family or partners (reported by 14% of participants), generally reflecting concern that the participant had or was at risk of acquiring HIV infection. The second most common event, reported by 3% of volunteers, was unintentional disclosure of participation in the trial. Each of the other potential problems was mentioned by fewer than 1% of participants.

During the trial, 368 volunteers became infected with HIV; 95% of this group provided information about negative social impacts after infection. Twelve reported a negative experience: Ten said that friends or relatives had blamed the vaccine for the infection or for increasing the participant's susceptibility to infection, one had been denied life insurance by an insurer that attributed his HIV status to his participation in the trial and one had been told that his participation made him ineligible to enroll in an unrelated clinical trial.

Seventeen percent of participants who reported a negative event answered questions about the degree to which these events affected their quality of life. Overall, 87% said that the experiences had minimal or moderate impact; this proportion includes 93% of those reporting interpersonal problems. However, four of the five who had had problems with health insurance, six of the 22 who had had employment difficulties and one of the four reporting problems with medical or dental care said that these experiences had had a significant impact on their quality of life.

Because 94% of the volunteers were men, researchers assessed predictors of negative experiences separately by gender. For women, they conducted only univariate analyses, which indicated two significant relationships: The likelihood of reporting negative social impacts was elevated early in the trial and among women enrolled at sites with fewer than 50 participants.

For men, however, they assessed predictors in a model controlling for participants' demographic characteristics and risk behaviors, characteristics of the enrollment site and timing of the interview. This analysis showed that the likelihood of reporting a negative experience was higher among men who were aged 18–25 or 26–35 at enrollment than among those aged 46 or older (odds ratios, 1.6 and 1.4, respectively), and higher among men who had had multiple partners shortly before entering the study than among those who had had none or one (1.3–1.4, depending on number). The odds of reporting a negative social impact were elevated for men at the sites with the fewest participants (2.3) and at sites in cities with the highest numbers of AIDS cases (1.4). Reports of negative experiences were less likely at the 12-month visit than at six months (0.5), and the differential increased at each successive visit (to 0.3 at 36 months).

The researchers find several important lessons in their results. One is the need for vaccine researchers to make clear to the public that HIV vaccines do not cause infection; another is the need for trial staff to discuss with volunteers whether and how to disclose their participation to family, friends and others. The unexpected finding that the likelihood of negative social events is elevated in AIDS epicenters suggests that "staff from these settings should not presume that living in a city heavily affected by HIV/AIDS translates to greater knowledge of HIV vaccines." In conclusion, the researchers remark that "these and other steps should support culturally appropriate efforts to protect the well-being of future vaccine efficacy trial volunteers."—*D. Hollander*

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